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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/171,885	10/28/1998	ROGER S. CUBICCIOTTI	BDA-0038	8594

7590 07/16/2002

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EXAMINER	
WARE, TODD	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 07/16/2002 26

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/171,885	Applicant(s) CUBICCIOTTI, ROGER S.	
	Examiner Todd D Ware	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-41* is/are pending in the application.

4a) Of the above claim(s) *30-33 and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *34-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of election filed 4-26-02 is acknowledged.

Election/Restrictions

1. Applicant's election with traverse of Group III, claim(s) 34-35 (and 36-40, see below), drawn to a method of making and administering a prodrug complex in Paper No. 25 is acknowledged. The traversal is on the ground(s) that the groups have at least one corresponding special technical feature –the ability to produce and administer prodrug complexes by first identifying a drug and then selecting a synthetic receptor that specifically binds to the drug. This is not found persuasive because the processes set forth in the groups are highly diverse highly complex processes that do not appear to be related or required by each other. For example, the process of *in vitro* evolution in essence is "evolution in a test tube" and involves evolving a population of nucleic-acid sequences under defined selection pressures by creating a randomized pool of nucleic acids and subjecting it to several rounds of selection (survival), amplification (reproduction), and mutation (introduction of genetic variation) that together are the analog of "generations" in natural populations. The process of combinatorial selection is based on the premise that the probability of finding a molecule in a random screening process is proportional to the number of molecules subjected to the screening process. Indeed, this screening process can be accomplished by several forms such as parallel chemical synthesis and testing of multiple individual compounds or compound mixtures in solution, synthesis and testing of compounds on solid supports, and biochemical or

organism-based synthesis of biological oligomer coupled to selection and amplification strategies. In other words, the claimed processes of producing a prodrug complex require diverse, unrelated experimentation that entail different paths to arrive at the prodrug complex. Furthermore, the state of the prior art is unpredictable and would vary greatly dependent upon the active agent sought. Applicant's comments that the additional language was added at the request of examiners are considered. However, no manner in which the claims were to be amended was agreed upon. Also, the resulting differences in the scope and magnitude of distinctness between the processes was known by the examiners during the interview of 8-23-01. Applicant's comments regarding claims 36-40 falling within the scope of Group III are persuasive and these claims will be examined in accordance with Group III in the instant Office Action.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 30-33, and 41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 25.

3. This application contains claims 30-33, and 41 drawn to an invention nonelected with traverse in Paper No. 25. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 34-40 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Morgan, Jr. et al (5,106,951; hereafter '951).

'951 discloses drug/carrier complexes and a method of administering a drug via a drug/carrier complex where a drug binds to a polymeric carrier to form a prodrug complex that is capable of allowing drug dissociation from the polymeric carrier such that the drug retains its ability to bind to a site on or within a target cell. The examiner takes the position that the "antibody csDBM complex" of '951 is considered an antibody fragment that makes up the synthetic receptor. Since '951 states that the drug's ability to bind to a higher affinity site on or within the target cell is retained (abstract; C4, L43-C5, L25; C8, L30-40; C18, L43-48), the conjugate of '951 binds preferentially to the "pathophysiologic receptor" (the higher affinity site on or within the target cell). '951 also discloses that the drug-conjugate is not exposed to derivatization conditions that might compromise the potency of the drug (i.e. the drug is immobilized and is protected from metabolism which would increase its half-life over administration of the drug alone) (C4, L43-50). '951 further discloses that targeting proteins may be attached to the conjugate.(C7, L10-19, 30-37). The carriers of '951 may also bind more than one drug (C10, L62-66). Column 5, lines 11-17 discloses the "csDBM is specifically designed to

fit the drug molecule and undergo multiple non-covalent interactions with a drug." Thus, the limitations reciting that the drug is specifically bound to the synthetic receptor via noncovalent interactions between the selected drug and the synthetic receptor are met by '951. The methods used to identify the conjugate are not considered patentably distinct as they are intended use limitations. Furthermore, the antibodies of '951 would be readily identifiable by the instant methods.

Response to Arguments

6. Applicant's arguments filed 5-3-01 have been fully considered but they are not persuasive. Applicant argues that the instant claims do not require the CsDBM of '951 and are therefore allowable over '951. However, this is not found persuasive since the antibody-CsDBM is considered to meet the "antibody-fragment" limitation of the instant claims, since no language excluding the CsDBM of '951 is included in the claims.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 34-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan, Jr. et al. (5,106,951; hereafter '951).

'951 teaches drug/carrier complexes and a method of administering a drug via a drug/carrier complex where a drug binds to a polymeric carrier to form a prodrug

complex that is capable of allowing drug dissociation from the polymeric carrier such that the drug retains its ability to bind to a site on or within a target cell. The "antibody csDBM complex" of '951 is considered the synthetic receptor. Since '951 states that the drug's ability to bind to a higher affinity site on or within the target cell is retained (abstract; C4, L43-C5, L25; C8, L30-40; C18, L43-48), the conjugate of '951 binds preferentially to the "pathophysiologic receptor" (the higher affinity site on or within the target cell). '951 also discloses that the drug-conjugate is not exposed to derivatization conditions that might compromise the potency of the drug (i.e. the drug is immobilized and is protected from metabolism which would increase its half-life over administration of the drug alone) (C4, L43-50). '951 further discloses that targeting proteins may be attached to the conjugate.(C7, L10-19, 30-37). The carriers of '951 may also bind more than one drug molecule (C10, L62-66). Column 5, lines 11-17 discloses the "csDBM is specifically designed to fit the drug molecule and undergo multiple non-covalent interactions with a drug." Thus, the limitations reciting that the drug is specifically bound to the synthetic receptor via noncovalent interactions between the selected drug and the synthetic receptor are met by '951. The methods used to identify the conjugate are not considered patentably distinct as they are intended use limitations. Furthermore, the antibodies of '951 would be readily identifiable by the instant methods.

'951 does not specifically state that the carriers of '951 may bind multiple drugs wherein the drugs are different. '951 does state that the carriers have multiple drug-binding regions capable of binding multiple drug molecules. Therefore, it would be obvious to one skilled in art at the time of the invention to design the conjugates of '951

wherein the domains would be different would be capable of binding more than one drug where the drugs are different with the expectation that administering more than one drug to treat a condition would result in an additive treatment effect with the motivation of protecting the drug against metabolism or other factors that might reduce potency.

Response to Arguments

9. Applicant's arguments filed 5-3-01 have been fully considered but they are not persuasive. Applicant reiterates arguments set forth in the rejection under 35 USC 102 that the instant claims do not require the CsDBM of '951 and are therefore allowable over '951. However, this is not found persuasive since the antibody-CsDBM is considered to meet the "antibody-fragment" limitation of the instant claims, since no language excluding the CsDBM of '951 is included in the claims.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Todd D Ware whose telephone number is (703) 305-1700. The examiner can normally be reached on 7:30 AM - 4 PM 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (703)308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

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July 13, 2002